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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/535,763

05/20/2005

Stefan Werner

049202/289226

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02/25/2011

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EXAMINER

PAGE, BRENT T

ART UNIT

PAPER NUMBER

1638

MAIL DATE

DELIVERY MODE

02/25/2011

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/535,763	Applicant(s) WERNER ET AL.	
	Examiner BRENT PAGE	Art Unit 1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 December 2010.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-5,11-14,17,18,23-27 and 29-31 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-5,11-14,17,18,23-27 and 29-31 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12/21/2010 has been entered.

Claims 1-5, 11-14, 17-18, 23, 25-27, and 29-31 are pending and examined herein on the merits.

Finality of the Office Action mailed out on 06/22/2010

Applicants urge that the Office Action mailed out on 06/22/2010 was improper, as the inclusion of Xu et al in the 103 rejection under obviousness was a new ground of rejection and request a withdrawal of finality in order to address this rejection (see pages 8-9 of response).

This is not persuasive because firstly, the rejection was not a new ground of rejection, but rather maintaining a previous ground of rejection. It is noted that none of the rebuttal to Applicants arguments relied upon Xu et al, and indeed, the rejection itself, did not rely upon Xu et al as it is clear that Xu et al is cited for a feature that is no longer in the claims. In order to clarify the case the obviousness rejection was repeated and the Examiner inadvertently repeated the rejection from an earlier round of prosecution. While the Examiner apologizes for this typographical error, as noted, and further contends that because Xu et al is unrelated to the claims as currently written and since no alteration or change

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from what was previously on record was made that requires a response, and since Xu was wholly unrelieved upon and unused in order to rebut the arguments, that there literally is no reason or ground upon which Applicants would need to respond and the finality, therefore of the previous office action is not withdrawn. The office action is repeated below with the proper correction of the typographical error and Applicants arguments are addressed accordingly.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-5, 11-14, 17-18, 23, 25-27, and 29-31 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Klimyuk et al (WO02088369) in view of Hooykaas et al (WO0189283).

The claims are broadly drawn to methods of controlling genetically modified multicellular organisms or parts thereof comprising providing any genetically modified plant or cell containing any heterologous nucleic acid encoding any protein causing expression of a polypeptide into cells of said genetically modified plant, wherein the plant or cells contain an additional heterologous nucleic acid that controls a cellular process of interest, wherein said nucleic acid encoding protein causes the expression of a protein from said

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heterologous nucleic acid wherein both the protein and polypeptide are a site-specific recombinase or an integrase..

Klimyuk et al (WO02088369, published 11/07/2002) teach a method for expressing a nucleic acid sequence of interest in plants providing at least two precursor vectors (claim 2 and meets the limitation of additional heterologous nucleic acid) wherein the processing of the precursor is by RNA splicing, ligation and recombination (claim 13), wherein the cell provides in trans functions necessary for replicon replication, virus particle assembly (claim 18), wherein the genetic engineering is done by virus or *Agrobacterium* mediated transfection wherein the process results in the expression of multiple genes of a biochemical pathway or cascade (claims 19 and 21 and 23) wherein the heterologous sequence is integrated stably into a host chromosome (claim 27), and wherein the heterologous nucleic acid introduced is a vector comprising TMV, a viral movement protein and the introduction of CRE into the cell, when jointly present with the LOX sites, commences RNA production from the amplicon (see Examples).

Klimyuk et al do not teach the direct introduction of the protein into the cell.

Hooykaas et al (WO0189283 published 05/21/2001) teach the translocation of the CRE polypeptide into plant cells using VirE2 and trans-splicing to achieve recombination to induce the transcription of a heterologous gene, NPTII, (See claims and Examples).

Given the state of the art and the disclosures by Kimyuk et al, and Hooykaas et al, it would have been obvious to one of ordinary skill in the art to modify the method taught by Kimyuk et al by using the system taught by Kimyuk et al to translocate recombinase into the cell as taught by Hooykaas et al and suggested by Kimyuk et al when stating "A serious concern with prior art virus-based plant expression systems is biological safety" expressing a long felt need to improve the safety of plant expression systems.

Several elements of the claims are well-known in the art and considered to be design choices. The intein trans-splicing method was known in the art at the time of invention, as was the VirE2 system of translocating polypeptides into plant cells. Further it is noted that the limitation of the claims only requires the second polypeptide to comprise "a" fragment of the first protein, and thus, an unspecified fragment may comprise any number of amino acids.

Response to Arguments

Applicant's arguments filed 12/21/2010 have been fully considered but they are not persuasive.

Applicants urge that Kimyuk et al do not teach a viral movement protein or part thereof (see pages 10-11 of response).

This is not persuasive because that particular element of the instant claims is currently remedied by Hooykaas et al as described in the previous office action wherein it was stated by the Examiner "In Hooykaas' system, the introduced polypeptide is capable of cell to cell movement and controls the plant process", meeting the limitations of the instant claims. Applicants have not

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argued that the combination of Hooykaas et al and Klimyuk et al do not contain this feature, and instead are relying on attacking the references individually. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Applicants urge that Hooykaas et al does not consider the nucleic acid of interest and therefore do not teach or suggest that both the fusion protein and the protein encoded by the heterologous nucleic acid should have enzymatic activity of a site-specific recombinase/integrase (see page 12 of response).

This is not persuasive, because as discussed in the Office Action mailed out on 06/22/2010, Hooykaas envisions both transferring the fusion protein and forming it by the transfer system itself, which arrives at the instant claims combination (see page 6 of Final Office Action mailed out on 06/22/2010).

Applicants urge that Hooykaas could not combine the above statement because even if Hooykaas transformed the plant with multiple vectors that the fusion protein could be expressed without the presence of the fusion protein and thus, the instant invention could not be arrived at (see pages 12-13 of response).

This is not persuasive because Applicants appear to be urging that in teaching an "either....or" language, Hooykaas effectively rules out the use of the fusion protein in combination with the vector. However, Hooykaas et al is not teaching away from the invention which is what Applicant appears to be urging,

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but rather, teaching two possible uses and methods of arriving at the expression of the fusion protein and expressing a heterologous nucleic acid. It is noted that the direct introduction of the fusion protein motivation and teaching is provided by Hooykaas et al, however, the safety features including the cascade effect of the instant invention and the requirement of CRE and LOX sites is actually provided by Klimyuk et al. In other words, Hooykaas et al is providing the delivery system and Klimyuk et al is providing the vector and heterologous gene of interest. Hooykaas et al also point out that CRE can be used in either situation and certainly does not teach away or provide any reason that one of ordinary skill in the art would doubt they could be successfully used together.

Applicants urge generally, that improper hindsight reconstruction has arrived at the present rejection of the claims as instantly written (see page 14 of response).

This is not persuasive because the claims as instantly written claim a method of using two known procedures for controlling gene expression in a cell, and furthermore, an acknowledgement that either procedure could be used. Applicants have not provided evidence of unexpected results, nor have Applicants provided reasoning that one of ordinary skill in the art would not have combined the two systems as currently written in the rejection of record. In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which

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was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). In the instant case, Applicants have not provided a reasoned statement to contradict that such knowledge was within the level of one of ordinary skill in the art at the time the invention was made.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BRENT PAGE whose telephone number is (571)272-5914. The examiner can normally be reached on Monday-Friday 8-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg can be reached on (571)-272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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Brent Page
Examiner
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